PATENT SPECIFICATION

978,265

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COMPLETE SPECIFICATION

NO DRAWINGS

Method for Coating Tablet.

We, ABBOTT LABORATORIES, a Corporation organized and existing under the laws of the State of Illinois, United States of America, of 14th Street and Sheridan Road, North Chicago, Illinois, County of Lake, State of Illinois, United States of America, do hereby declare the invention, for which we pray that a patent may be granted to us, and the method by which it is to be performed, to be particularly described in and by the following statement:—

This invention relates to tablet coatings and to a method of obtaining a pharmaceutically elegant tablet. More particularly, this invention relates to the use of hydroxypropyl methylcellulose and ethylcellulose to obtain a polished or glossy finish on a tablet previously air-coated with a colored coating.

The tablet coating art has recently become aware of the advantages of employing the air-coating method for applying coating solutions to tablets. Among the many advantages is the elimination of the familiar coating pans and drying ovens, not to overlook the time saving element. An example of such a method for air-coating tablets is described in U.S. 2,648,609. Another technique for applying a coating solution by the air-coating method is described in co-pending Application No. 6533/61 (Serial No. 978,264).

It is well recognized in the tablet coating art that a coating should have a glossy finish in order to have a pleasing appearance. When the pan-coating method is employed, the coatings do have such a gloss. This is accomplished by the buffing action of the tablets occurring in the pan. On the other hand, when an air-coating method is employed, the tablets receive no buffing action and consequently the finish on the tablet is dull and unattractive. This is true whether a plastic film-coating as described in U.K. Specification No. 762,229, or a standard sugar coating, is applied to the tablets. Further, whether the tablets be coated with a plastic film or a sugar coating, or whether the coating is applied by the pan or the air-coating method, the coatings are sensitive to high temperatures and humidity upon storage and become tacky.

It is, therefore, an object of the present invention to provide a gloss on a tablet by the air-coating method.

It is another object of this invention to provide a tablet coating which is resistant to high temperatures and moisture upon storage.

According to the present invention there is provided a method of obtaining a gloss and a protective coat on coated tablets characterised by the steps of: formulating a fluid coating composition with a glossing agent selected from the group consisting of hydroxypropyl methylcellulose containing 5-15% by weight of 2-hydroxypropoxyl groups and 27-32% by weight of methoxyl groups, ethylcellulose containing 42-49.5% by weight of ethoxyl groups, mixtures of said hydroxypropyl methylcellulose and said ethylcellulose, and a non-aqueous solvent for said glossing agent; and air-coating said coating composition onto said tablets to coat said tablets with said coating composition and to dry said fluid coating composition on said tablets.

Preferably the fluid coating composition includes a film-forming polymer other than said glossing agent and the non-aqueous solvent for the film-forming polymer and the glossing agent.

Advantageously the fluid coating composition includes a plasticiser and the non-aqueous solvent is a solvent for the plasticiser and the glossing agent.

The film coating composition may include both ethylcellulose and hydroxypropyl methylcellulose, the ethylcellulose being present in the composition in the ratio of 3 parts by weight per part by weight of hydroxypropyl

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methylcellulose.

In one embodiment the composition to be air-coated on to the tablets comprises carboxylated polyvinyl acetate copolymer having 3-5% carboxyl groups and a molecular weight range of approximately 45,000 to 100,000, hydroxypropyl methylcellulose containing 5-15% by weight of 2-hydroxypropoxyl groups and 27-32% by weight of methoxyl groups, said carboxylated copolymer and said hydroxypropyl methylcellulose being present in a ratio of between 1:1 and 1:10 parts by weight, and a non-aqueous solvent for said carboxylated polyvinyl acetate copolymer and said hydroxypropyl methylcellulose.

Triethyl citrate may be included as a plasticising agent, in a range between 0.1-10% w/v of the fluid composition in which case the non-aqueous solvent is also a solvent for the plasticising agent.

In an alternative embodiment of the invention the composition to be air-coated on to the tablets comprises polyvinylpyrrolidone, ethylcellulose containing 42-49.5% by weight of ethoxyl groups, an ethyleneoxide-polypropylene glycol condensation product, and a non-aqueous solvent for said compounds, the ethylcellulose and polyvinylpyrrolidone being present in a ratio of between 1:100 and 2:1 parts by weight and the glycol condensation product being present in a range of between 0.1-5% w/v of the fluid composition.

The cellulose coating composition is applied by the air-application method after a colored coating material is applied to a tablet and dried. Any of the known methods for the air-application of coating compositions, wherein a fluidized bed of tablets is maintained and the coating composition is introduced in the form of a spray, can be employed. However, the method disclosed in Applicants' co-pending Application No. 6533/61 (Serial No. 978,264) is preferred. Briefly stated, that method comprises the forming of a columnar bed of tablets to be coated wherein the bed is preferably greater in height than it is in the horizontal cross-sectional dimension. An air stream is directed upwardly through a portion of this bed with sufficient force that the tablets in that portion move upwardly forming a fluidized spout of tablets up through the spout portion. The spout extends above the top of the bed with the tablets falling therefrom back onto the top of the bed. In the parts of the bed adjacent the spout, the tablets move downwardly. The cellulose coating material is atomized and introduced into the upwardly moving stream of air. The atomized cellulose fluid is deposited on the tablets in the upwardly moving spout with the deposited liquid being dried by the air.

As stated above one of the cellulose derivatives employed in this invention which serves as a glossing agent is hydroxypropyl methylcellulose containing 5-15% by weight of 2-hydroxypropoxyl groups and 27-32% by weight of methoxyl groups. The other cellulose derivative is ethylcellulose containing 42-49.5% by weight of ethoxyl groups. The terms "hydroxypropyl methylcellulose" and "ethylcellulose", or the combination thereof, as hereinafter used, is meant to refer to the specific derivatives and weight proportions of substituent groups as previously designated for these compounds.

The following examples illustrate the formulation of the coating solutions employed in this invention. The purpose of the examples is to describe the invention more fully and it should be understood that the invention is not intended in any way to be limited thereby. In the following examples, the viscosity of both hydroxypropyl methylcellulose and ethylcellulose is 50 cps., i.e., for the hydroxypropyl methylcellulose from a 2% weight by weight solution in water and for the ethylcellulose from a 5% weight by weight solution in 60.40 by weight toluene-ethanol.

EXAMPLE I

A tablet coating solution is prepared according to the following formula:

Hydroxypropyl methylcellulose, 50 cps.	20.0 gm.
Equal volumes of methylene chloride and Absolute Ethanol q.s.a.d.	1.0 liter

The hydroxypropyl methylcellulose is added with agitation to a portion of equal parts of the methylene chloride and the ethanol. The remainder of the methylene chloride and the ethanol is thereafter added and the mixture thoroughly stirred.

The resulting coating solution is applied to a 4 kg. batch of tablets by means of the air-coating method described in Applicants' co-pending Application No. 6533/61 (Serial No. 978,264), as previously outlined. The tablets are convex in shape and are compressed on a 5/16" punch with 10 tablets weighing 1.78 grams. A plastic colored, film coating is previously applied by this air-coating method to the tablets. The previously coated tablets have a dull appearance but after the tablets are coated with the hydroxypropyl mehylcellulose solution, a pleasing gloss is obtained.

EXAMPLE II

A coating solution for tablets is prepared according to the following formula:

Hydroxypropyl methylcellulose, 50 cps.	15.0 gm.
Ethylcellulose, 50 cps.	5.0 gm.
Equal volumes of methylene chloride and Absolute Ethanol q.s.a.d.	0.1 liter

The hydroxypropyl methylcellulose and the

ethylcellulose are added with agitation to a portion of equal parts of the methylene chloride and the ethanol. The mixture is stirred until the ethylcellulose and the hydroxypropyl methylcellulose are completely dissolved. The remainder of the methylene chloride and the ethanol is added with stirring. The resulting coating solution is applied as a finishing coat to previously coated tablets, as described in Example I.

EXAMPLE III

In this example a film-forming copolymer, as represented by carboxylated polyvinyl acetate copolymer having 3.5% carboxyl groups, is employed as a film-forming copolymer in conjunction with hydroxypropyl methylcellulose. The copolymer is a preferred film-forming polymer and is preferably employed in a ratio of between 1:1 and 1:10 parts by weight of an hydroxypropyl methylcellulose. The film-forming copolymer of this example has a molecular weight range of approximately 45,000 to 100,000, a viscosity range of 8-35 cps. in an 8.6% w/v solution of ethanol and a softening point range of 123-180°C. The carboxylated polyvinyl acetate copolymer when applied as a coating solution to a tablet forms a thin film of plastic on the tablet.

The fluid coating composition is prepared according to the following formula:

Hydroxypropyl methylcellulose	16.0 gm.
Carboxylated polyvinyl acetate copolymer	4.0 gm.
Equal volumes of methylene chloride and Absolute Ethanol q.s.a.d.	1.0 liter

The hydroxypropyl methylcellulose and the carboxylated polyvinyl acetate copolymer are added with agitation to a portion of equal prats of the methylene chloride and the ethanol. The remainder of the methylene chloride and the ethanol is thereafter added and the mixture is thoroughly stirred. The resulting coating solutions is applied as described in Example I.

EXAMPLE IV

In this example a plasticizer, as represented by triethyl citrate, is employed with the coating composition of Example 3. The fluid coating composition has the following formula:

Hydroxypropyl methylcellulose	12.0 gm.
Carboxylated polyvinyl acetate copolymer	12.0 gm.
Triethyl citrate	10.0 gm.
Equal volumes of methylene chloride and Absolute Ethanol q.s.a.d.	1.0 liter

The ingredients in this example are combined in the manner outlined in Example III with the triethyl citrate being added with agitation to the solvents along with the hydroxypropyl methylcellulose and the carboxylated polyvinyl acetate copolymer. The coating solution is applied as described in Example I.

The following example illustrates the use of a plasticizer in conjunction with ethylcellulose along with the addition of a film-forming polymer as represented by polyvinylpyrrolidone. Polyvinylpyrrolidone is a preferred film-forming polymer and the preferred ratio of ethylcellulose to polyvinylpyrrolidone is between 1:100 and 2:1 parts by weight.

EXAMPLE V

A solution for use in coating tablets in accordance with the method of the present invention was prepared according to the following formula:

Polyvinylpyrrolidone	80.0 gm.
Ethylcellulose, 50 cps.	6.0 gm.
Pluronic (Registered Trade Mark) F-68	10.0 gm.
Acetone	0.8 liter
Absolute ethanol, q.s.a.d.	1.2 liters

The polyvinylpyrrolidone, ethylcellulose and the Pluronic F-68 are dissolved with agitation in a mixture of the acetone and a portion of the ethanol. When the foregoing ingredients are completely dissolved the balance of the ethanol is added. The resulting solution is applied to previously coated tablets as described in Example I.

Pluronic F-68 is employed in this example as a plasticizer. The chemical composition of Pluronic F-68 is described in U.K. Specification No. 785,387 and is an ethylene oxidepolypropylene glycol condensation product, and is preferably present in a ratio of 0.1 to 5% w/v of the fluid composition. It should be understood that other plasticizers as for example, glycerine, propylene, glycol, polyethylene glycols, ethyl phthalyl ethyl glycolate, butyl phthalyl butyl glycolate, acetyl triethyl citrate and similar plasticizing agents can be employed. Examples I, II and III do not illustrate the use of such plasticizers but they can be employed as described in Examples IV and V, if desired.

Also, other solvent combinations can be employed in Examples I and II for example, benzene-ethanol, chloroform-ethanol, ethyl lactate-ethanol and methyl salicylate-ethanol. In a like manner, other solvents can be employed in Example V as represented by ethanol and methylene-chloride-ethanol.

It should be understood that if desired, various film-forming polymers and copolymers other than polyvinylpyrrolidone and carboxylated polyvinyl acetate copolymer can be employed in conjunction with ethylcellulose as well as hydroxypropyl methylcellulose and combinations thereof. When a solution of a film-forming polymer in a suitable solvent is applied to a glass plate, a coherent film can be peeled off the glass after

evaporation of the solvent, and the term "film-forming polymer" used in this Specification means a polymer having this property. The following are representative of such film-forming polymers: cellulose acetate; cellulose acetate derivatives, as for example, cellulose acetate phthalate; cellulose acetate propionate, cellulose acetate butyrate; maleic anhydride-ethylene copolymers; carboxylated styrene copolymers; ethylene oxide copolymers; polyvinylpyrrolidone-vinyl acetate copolymers; polyvinyl acetate copolymers; lower alkyl methacrylates; copolymers of lower alkyl acrylates with lower alkyl methacrylates; and copolymers of lower alkyl methacrylates with methacrylic acid. In the same manner, a water soluble wax as represented by polyethylene glycol can also be employed.

By use of this invention, a uniform exterior coating is applied, by means of air-application to tablets, providing the tablet with a polished glossy finish. The exterior coating gives an elegant appearance to the tablet which could otherwise be achieved only by pan coating and polishing the tablet with waxes or the like. The application of the formulations herein described by the pan coating method is not feasible since the resulting tablets are sticky and tend to adhere to each other. Thus, by use of the claimed method, the entire coating operation can be performed in the same air-coating unit. The glossy coating not only has aesthetic value but also serves as a seal to protect the colored coating from deleterious storage conditions.

WHAT WE CLAIM IS:—

1. A method of obtaining a gloss and a protective coat on coated tablets characterised by the steps of: formulating a fluid coating composition with a glossing agent selected from the group consisting of hydroxypropyl methylcellulose containing 5-15% by weight of 2-hydroxypropoxyl groups and 27-32% by weight of methoxyl groups, ethylcellulose containing 42 to 49.5% by weight of ethoxyl groups, mixtures of said hydroxypropyl methylcellulose and said ethylcellulose, and a non-aqueous solvent for said glossing agent; and air-coating said coating composition onto said tablets to coat said tablets with said coating composition and to dry said fluid coating composition on said tablets.

2. A method according to claim 1 wherein the fluid coating composition includes a film-forming polymer, other than said glossing agent, and the non-aqueous solvent is a solvent for the film-forming polymer and the glossing agent.

3. A method according to claim 1 or 2 wherein the fluid coating composition includes a plasticiser and the non-aqueous solvent is a solvent for the plasticiser and the glossing agent.

4. A method according to any of claims 1 to 3 wherein the film coating composition includes both ethylcellulose and hydroxypropyl methylcellulose, the ethylcellulose being present in the composition in the ratio of 3 parts by weight per part by weight of hydroxy-propyl methyl cellulose.

5. A method according to any of claims 1 to 4 wherein the fluid coating composition includes carboxylated polyvinyl acetate copolymer as a film-forming polymer and the non-aqueous solvent is a solvent for said polymer.

6. A method according to claim 5 wherein the carboxylated copolymer and the hydroxypropyl methylcellulose are present in the fluid coating composition in a ratio of between 1:1 and 1:10 parts by weight.

7. A method according to claim 6 wherein the carboxylated copolymer has 3-5% carboxyl groups and a molecular weight range of about 45,000 to 100,000.

8. A method according to any of claims 1 to 7 wherein the fluid coating composition includes triethyl citrate as a plasticising agent and the non-aqueous solvent is a solvent for said plasticising agent.

9. A method according to any of claims 1 to 4 wherein the fluid coating composition includes polyvinylpyrrolidone as a film-forming polymer.

10. A method according to claim 9 wherein the fluid coating composition includes an ethylene oxide-polypropylene glycol condensation product as a plasticising agent and the non-aqueous solvent is a solvent therefor.

11. A method according to claim 9 or claim 10 wherein the ethylcellulose and polyvinylpyrrolidone are present in a ratio of between 1:100 and 2:1 parts by weight.

12. A method according to claim 10 or claim 11 wherein the glycol condensation product is present in a ratio of 0.1 - 5% w/v of the fluid composition.

13. A method according to any of claims 5 to 12 wherein said composition comprises carboxylated polyvinyl acetate copolymer having 3 - 5% carboxyl groups and a molecular weight range of approximately 45,000 to 100,000, hydroxypropyl methylcellulose containing 5 - 15% by weight of 2-hydroxypropoxyl groups and 27 - 32% by weight of methoxyl groups, said carboxylated copolyer and said hydroxypropyl methylcellulose being present in a ratio of between 1:1 and 1:10 parts by weight, and a non-aqueous solvent for said carboxylated polyvinyl acetate copolymer and said hydroxypropyl methylcellulose.

14. A method according to claim 13 wherein triethyl citrate is included in the composition as a plasticising agent, in a range between 0.1 - 10% w/v of the fluid composition and the non-aqueous solvent is

a solvent for said plasticising agent.

15. A method according to any of claims 5 to 14 wherein said composition comprises polyvinylpyrrolidone, ethylcellulose containing 42 - 49.5% by weight of ethoxyl groups, an ethyleneoxide-polypropylene glycol condensation product, and a non-aqueous solvent for said compounds, the ethylcellulose and polyvinylpyrrolidone being present in a ratio of between 1:100 and 2:1 parts by weight and the glycol condensation product being present in a range of between 0.1 - 5% w/v of the fluid composition.

16. A method according to any of claims 1 to 15 wherein the composition is air-coated into the tablets by means of a fluidized bed.

17. A method of providing a gloss on air-coated tablets substantially as herein described.

18. Tablets having a glossed, protective coat applied by the method of any of claims 1 to 17.

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